

Remarks/Arguments

Status of the Application

In the Non-Final Office Action mailed September 22, 2006, claims 1, 2, 4, 6, 15, 17, and 19 were rejected. In the present response, claims 1, 2, 4, 6, and 15 have been amended; and claims 27-34 have been added so that claims 1, 2, 4, 6, 15, 17, 19, and 27-35 are pending. Support for the newly added claims can be found in the claims as originally filed and/or Examples 55-57. No new matter has been added.

The cross-referencing statement inserted via the preliminary amendment filed December 9, 2003 has been amended to indicate U.S. application no. 10/222,990, filed August 19, 2002, issued as Patent No. 6,693,117. In addition, Applicants have reformatted the aforementioned cross-referencing statement via additional amendments noted hereinabove. Applicants submit the amendments made to the cross-referencing statement are not substantive in nature.

The remaining amendments to the specification are being made to correct typographical errors associated with 1) inadvertently omitting the comma between substituent groups $-(CH_2)_pCH_3$ and $-(CH_2)_pSOR^5$, $-(CH_2)_qCH_3$ and $-(CH_2)_qSOR^5$, and $-(CH_2)_rCH_3$ and $-(CH_2)_rSOR^5$; 2) identifying the substituent $-(CH_2)_pSOR^5$ as $-(CH_2)_pSOR^5R^4$; 3) identifying the substituent $-(CH_2)_pSO_2NR^5R^4$ as $-(CH_2)_pSO_2NR^5$; 4) identifying the substituent $-(CH_2)_qSOR^5$ as $-(CH_2)_qSOR^5R^4$; and 5) identifying the substituent $-(CH_2)_qSO_2NR^5R^4$ as $-(CH_2)_qSO_2NR^5$. The amendments are not being made for reasons related to patentability but rather simply to correct typographical errors.

The claims were amended throughout to accommodate the above-identified amendments to the specification. The claims were further amended throughout for reasons related to grammar and clarity. Such amendments are not being made for reasons related to patentability but rather to correct typographical errors and bring further clarity to the claims. No new matter has been added.

35 USC §112, first paragraph

The Office rejected claims 1, 2, 4, 6, 15, 17, and 19 under 35 U.S.C. 112, first paragraph "because the specification, while being enabled for R's to a H, does not reasonably provide enablement for all the various substitutions and optionally substituted groups." The Office further alleges that the "specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." The Office relied on the following in *In re Wands*

factors in making this rejection: 1) the breadth of the claims; 2) the nature of the invention; 3) the state of the prior art; 4) the level of one of ordinary skill in the art; 5) the level of predictability in the art; 6) the amount of direction provided by the inventor; 7) the existence of working examples; and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. 858 F.2d 731 (Fed. Cir. 1988).

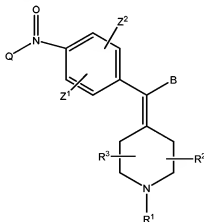
Applicants, however, respectfully assert the Office has failed to establish a *prima facie* case of nonenablement because Applicants' application as-filed enabled a person skilled in the pharmaceutical arts to use the full scope of the invention being claimed. Applicants further assert that such a result is inevitable when the evidence regarding each of the In re Wands factors is, in accordance with MPEP Section 2164.01(a), properly weighed. Indeed, as Section 2164.01(a) of the MPEP expressly indicates, "The determination that 'undue experimentation' would have been needed to make and use the claimed invention is not a single, simple factual determination"...but, "[r]ather, it is a conclusion reached by weighing all the above noted In re Wands factual considerations."

Applicants now turn to the arguments relied on by the Office in rejecting Claims 1, 2, 4, 6, 15, 17, and 19 as allegedly nonenabled.

Breadth of the Claims

With regard to the breadth of the claims, the Office asserts that the "instant claims encompass many compounds from an aromatic carbocyclic moiety ... having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings." The Office further asserts that "these compounds cover a wide range of compounds" and that "it is unclear from the claims what is encompassed."

Applicants, however, respectfully assert that the breadth of Claim 1, which is the broadest claim, is limited to the following core genus:



wherein

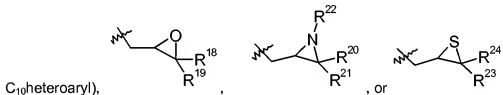
B is an optionally substituted phenyl or naphthyl;

Q is an optionally substituted C₅-C₆hydroaryl, C₅-C₆heterohydroaromatic, C₅-C₆cycloalkyl, or C₅-C₆heterocycloalkyl;

R² and R³ are selected from H and C₁-C₆alkyl;

Z¹ and Z² are selected from H, CH₃, -(CH₂)_rCF₃, halogen, -CONR⁶R⁷, -CO₂R⁶, -COR⁶, -(CH₂)_rNR⁶R⁷, -(CH₂)_rCH₃, (CH₂)_rSOR⁶, -(CH₂)_rSO₂R⁶ and -(CH₂)_rSO₂NR⁶R⁷, wherein r is 0, 1, or 2; and

R¹ is H, branched or straight C₁-C₆ alkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, (C₁-C₂alkyl)-(C₃-C₆cycloalkyl), optionally substituted C₆-C₁₀ aryl, optionally substituted C₅-C₁₀heteroaryl, optionally substituted (C₁-C₂ alkyl)-(C₆-C₁₀ aryl), optionally substituted (C₁-C₂ alkyl)-(C₅-



The breadth of Claim 2 is directed to Formula I compounds wherein Q is a morpholine, piperidine, or pyrrolidine; R¹ is a H, a branched or straight C₁-C₄ alkyl, C₃-C₅ cycloalkyl, (C₁-C₂alkyl)-(C₃-C₆cycloalkyl), an optionally substituted C₆-C₁₀aryl, or an optionally substituted C₅-C₆heteroaryl; and R² and R³ are selected from H and CH₃.

Finally, the breadth of claim 4 is directed to specific compounds encompassed by Formula I. The specific compounds claimed in claim 4 are exemplified in working examples 55-57, which are set forth at page 83, line 2 to page 84, line 16.

Applicants respectfully assert that the scope of the claims at issue is readily discerned from the outline of the claims set forth herein. Applicants further assert that the scope of the claims at issue is not unreasonable when the claims are viewed by a person of ordinary skill in the pharmaceutical arts in light of what is disclosed in the specification and examples as originally filed. Accordingly, Applicants respectfully assert that the scope of enablement provided by the application to one skilled in the art as of the date such application was filed is commensurate in scope with the scope of protection sought by the claims at issue.

Nature of the Invention

With regard to the nature of the invention, the Office asserted "the invention is a compound for pharmaceutical use."

Applicants acknowledge the compounds claimed herein are for pharmaceutical use. Applicants, however, respectfully assert a person of ordinary skill in the pharmaceutical arts would have known, as of the filing date of the application at issue, the scope of the invention being claimed herein.

State of the Prior Art

With regard to state of the prior art, the Office asserted "the pharmaceutical art is highly unpredictable". The Office further asserted that "compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine"; "[o]ne of them is a bronchodilator and they differ only by a methyl group." The Office concluded "these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face."

Applicants, however, have not asked one of ordinary skill in the art to accept the claimed invention on its face. Rather, Applicants have described the invention claimed herein in terms commensurate in scope with the breadth of the claims at issue. Indeed, as already mentioned hereinabove, specific compounds encompassed by the claims at issue are set forth in Examples 55-57 and Scheme 7, which are disclosed at page 80, line 17 to page 84, line 16. Moreover, in light of what was disclosed in Examples 55-57, the specification at page 2, line 15 to page 7, line 13, and Examples 1-54 and 58-68, Applicants respectfully assert that a person of ordinary skill in the pharmaceutical arts would have, at the time the application was filed, fully appreciated the scope of the claimed invention.

Level of Ordinary Skill in the Art

As the Office correctly noted, "[t]he ordinary artisan is highly skilled."

Accordingly, Applicants respectfully assert that Applicants' specification, when viewed in light of what was known in the art at the time the present application was filed, enabled the highly skilled persons of ordinary skill in the pharmaceutical arts to make and use the full scope of the presently claimed invention.

Level of Predictability in the Art

The Office asserts that "since the pharmaceutical art is highly unpredictable, it requires each embodiment to be individually assessed for physiological activity." The Office relies on *In re Fisher*, 427 F.2d 833 (CCPA 1970) for the proposition that "the more unpredictable the area is, the more specific enablement is necessary in order to satisfy the statute."

As MPEP section 2164.03 explains, "[t]he 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention." MPEP section 2164.03 further explains that "[t]he scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required."

As pointed out hereinabove Applicants have provided 3 working Examples, i.e. examples 55-57 that are specifically encompassed by the claims at hand. In addition to Examples 55-57, Applicants disclosed Examples 1-54 and 58-68, which are structurally similar to the compounds being claimed herein. In light of the structural similarities of such compounds and the guidance offered by the MPEP, Applicants respectfully assert that a person of ordinary skill in the pharmaceutical arts—whom the Office has already acknowledged is highly skilled—would be capable of extrapolating the information disclosed regarding the structurally similar compounds to the genus of compounds claimed herein.

Direction or Guidance

With regard to direction or guidance, the Office claims "[t]he inventor provides very little direction in the instant application"; "[t]here are few examples and they do not cover the scope of the substitutions and their optionally substituted groups."

Again, as already pointed out hereinabove, Applicants disclosed Examples 55-57 at page 83, line 2 to page 84, line 16, which are specifically encompassed by the genus claimed herein, and Scheme 7 at page 80, line 17 to page 82, line 29, which is a process for making the compounds of Examples 55-57. Applicants further disclosed a process for making compound (51) of Scheme 7 in Scheme 6 at page 55, line 1 to page 58, line 16. Accordingly, Applicants respectfully assert the information disclosed in the application as filed provides adequate guidance to the highly skilled person of ordinary skill in the pharmaceutical arts to make and use the full scope of the claimed invention.

Working Examples

With regard to working examples, the Office alleges that the "instant specification does not have example [sic] commensurate with the scope of the claimed invention"; "[t]he more unpredictable the art the more examples are required."

Applicants note that MPEP Section 2164.02 expressly states the following:

For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in

the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

Applicants again direct the Office's attention to Examples 55-57 (disclosed at page 83, line 2 to page 84, line 16), which are directed to specific compounds encompassed by the genus claimed herein; Scheme 7 (disclosed at page 80, line 17 to page 82, line 29), which is directed to a process for making the compounds of Examples 55-57; and Scheme 6 (disclosed at page 55, line 1 to page 58, line 16), which is directed to a process for making compound (51) of Scheme 7. Applicants respectfully assert that reading the claims at issue in light of Examples 55-57; Schemes 6 and 7; the general description of the invention set forth at page 2, line 15 to page 7, line 13; and Examples 1-54 and 58-68, would enable a highly skilled person of ordinary skill in the pharmaceutical arts to make and use the full breadth of the claims at issue without undue experimentation.

Quantity of Experimentation Needed

With regard to the quantity of experimentation needed, the Office argued that "[s]ince there are no working examples, the amount of experimentation is very high and burdensome."

Applicants, however, again note that there are 68 working examples—3 of which (Examples 55-57) are specifically encompassed by the claims at issue. Accordingly, Applicants respectfully assert in light of Examples 55-57; Schemes 6 and 7; the general description of the invention set forth at page 2, line 15 to page 7, line 13; and Examples 1-54 and 58-68 that any additional experimentation the Office believes the highly skilled person of ordinary skill in the pharmaceutical arts may need to perform to enable the full scope of the claims at issue would not be undue.

In sum, Applicants respectfully assert the Office has failed to establish a *prima facie* case of nonenablement because Applicants' application as-filed enabled a person skilled in the pharmaceutical arts to make and use the full scope of compounds encompassed by Formula I. Moreover, Applicants respectfully assert that such a conclusion is inevitable when each of the In re Wands factors is properly evaluated and weighed. Accordingly, Applicants respectfully request the Office to withdraw this rejection.

SUMMARY

In view of the foregoing amendments and remarks, Applicants respectfully submit that the application is in condition for allowance and respectfully solicit a Notice of Allowance of the claims at issue. In order to expedite disposition of this case, the Office is invited to contact Applicants' representative at the telephone number below to resolve any remaining issues. Although Applicants believe no fees are due, the Commissioner is hereby authorized to charge any deficiency in the fees or credit any overpayment to deposit account No. 26-0166, referencing Attorney Docket No. A1570-4P US.

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